The American Journal of Pathology, Vol. 183, No. 1, July 2013

The American Journal of
PATHOLOGY
ajp.amjpathol.org

This Month in *AJP*

IκB Kinase-β Limits Immediate Hypersensitivity

Pharmacological inhibitors of IκB kinase (IKK), especially IKK-β, have been developed to treat inflammatory diseases. Using a murine allergic conjunctivitis model, Miyazaki et al (**Am J Pathol 2013, 183:96–107**) analyzed the effects of such pharmacological inhibition of IKK on mast cell–mediated immediate hypersensitivity reactions. *In vitro* and *in vivo* analysis revealed that IKK-β limits B cell–mediated mast cell activation and inflammatory cytokine induction in immediate hypersensitivity by counter-balancing the activity of IKK-α.

Bisphenol A Causes Molar Incisor Hypomineralization

Molar incisor hypomineralization (MIH) in children occurs concurrently with endocrine disrupting chemical (EDC)–related pathologies. Jedeon et al (**Am J Pathol 2013, 183:108–118**) investigated the effect of bisphenol A (BPA), a typical EDC used in plastics and epoxy resin production, on amelogenesis in rats. Results document the first experimental MIH model and suggest that BPA exerts its effects on amelogenesis by disrupting normal protein removal from the enamel matrix, making MIH a marker for retrospective analysis of infant exposure to EDCs.

Progenitors in Fibrotic Liver Regeneration

Failure of fibrotic liver to regenerate after resection limits therapeutic options and increases demand for liver transplantation, posing a significant clinical problem. To gain insight into molecular mechanisms of regeneration in the context of fibrotic liver, Kuramitsu et al (**Am J Pathol 2013, 182–194**) characterized a murine model of partial hepatectomy of fibrotic liver and established a sequence of pathologic events associated with compromised fibrotic liver regeneration. Data suggest for the first time that therapeutic targeting of the profibrogenic progenitor (oval)–cell response represents a promising strategy to improve hepatectomy outcomes in patients with liver fibrosis.

Role of Reversal Cells in Osteoporosis

Osteoporosis may result from a failure during the bone formation phase that leads to incomplete refilling of resorption cavities or a failure at the reversal phase, uncoupling bone formation from resorption. Andersen et al (**Am J Pathol 2013, 235–246**) hypothesized that reversal cells may play a role in coupling bone resorption and formation. Data suggest that arrested reversal cells reflect aborted remodeling cycles that did not progress to the bone formation step. It is likely that bone loss in postmenopausal osteoporosis may result from both a failure of the bone formation step as commonly believed and a failure at the reversal step.

Tamoxifen Elicits Atheroprotection Not Reendothelialization

Tamoxifen, a drug used for hormonotherapy of estrogen receptor (ER)–positive breast cancers, has been proposed to have cardiovascular benefits. Using a mouse model deficient for ERα (*ERα*$^{-/-}$*LDL-r*$^{-/-}$) or selectively deficient for its activating function (AF)–1 (*ERαAF-1*$^{0/0}$*LDL-r*$^{-/-}$), Fontaine et al (**Am J Pathol 2013, 304–312**) determined the involvement of ERα and AF-1 in mediating vasculoprotective action of tamoxifen. Tamoxifen appears to mediate its actions *in vivo* through the selective activation of ERαAF-1, which is sufficient to prevent atheroma but not to accelerate endothelial healing.

http://dx.doi.org/10.1016/j.ajpath.2013.04.026